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Mapping the Landscape and Evolution of Drug Delivery for Glioma: A Bibliometric and Visual Analysis

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Abstract

Objectives:

This study aims to systematically analyze the intellectual landscape and evolving trends in glioma drug delivery research, and thematic shifts to inform future research directions.

Methods:

A bibliometric analysis was performed on articles indexed in the Web of Science Core Collection (WoSCC). Data were retrieved via a systematic search using the Boolean query: TS=(("glioma" OR "glioblastoma" OR "GBM")) AND TS=("drug delivery"), covering the period from January 1, 2015, to December 31, 2025. Data processing and visualization were conducted using VOSviewer, CiteSpace, and the Bibliometrix R package. Specifically, we analyzed publication metrics (volume, citations), geographical contributions (top countries, collaboration networks), author and institutional outputs (core authors, institutions), and thematic trends (keyword co-occurrence, theme classification). Key indicators including publication volume, citation impact, collaboration patterns, and thematic evolution were quantified to comprehensively characterize the research landscape of glioma drug delivery.

Results:

A total of 2,026 articles published in 446 journals were included, contributed by 11,135 authors. The field exhibited an annual growth rate of 6.39% and an international collaboration rate of 25.81%. China (811 articles) and the USA (291 articles) were the leading countries, with Fudan University (99 articles) and the Chinese Academy of Sciences (65 articles) as the top institutions. The Journal of Controlled Release (101 articles) was the most productive journal, while ACS Nano demonstrated the highest per-article citation impact. Dominant research themes included glioblastoma, drug delivery, blood-brain barrier (BBB), nanoparticles, temozolomide, and emerging frontiers such as exosomes, immunotherapy, and engineered exosome-mediated delivery. The field showed a clear upward trend in the number of articles published annually from 2015 to 2025, with research focus evolving from conventional nanocarrier design and chemotherapy delivery toward advanced strategies including exosomes/extracellular vesicles, immunotherapy, and targeted BBB-penetrating delivery systems.

Conclusions:

This bibliometric analysis demonstrates that glioma drug delivery research is steadily advancing toward precision theranostics with a maturing knowledge structure focused on intelligent nanocarriers. Global outputs are dominated by China and the United States, with research themes evolving from conventional nanocarriers to biomimetic systems, exosomes, and immunotherapy. Future studies may prioritize AI-assisted design and immunomodulatory strategies to address translational barriers. This work provides a comprehensive reference for guiding subsequent research in this field.

Keywords: Glioma, Drug delivery, Bibliometrics, Visual Analysis, Web of Science Core Collection

1 Introduction

Glioma, especially glioblastoma multiforme (GBM), remains a formidable challenge in neuro-oncology owing to its high malignancy, frequent recurrence, and pronounced therapeutic resistance. The current standard treatment, which combines surgical resection, radiotherapy, and temozolomide (TMZ) chemotherapy, faces considerable limitations. These are largely due to the selective barrier function of the blood-brain barrier (BBB) and the complex tumor microenvironment (TME). Elements such as hypoxic regions, acidic pH, immunosuppressive cell infiltration, and elevated interstitial fluid pressure collectively create substantial physical and biological obstacles to effective drug delivery.[1-4] In response, drug delivery systems (DDS) have emerged as a promising strategy. Recent years have seen the development of various functionalized carriers, including transferrin- or lactoferrin-modified liposomes, integrin-targeted polymeric micelles, pH-responsive mesoporous silica nanoparticles, and engineered exosomes.[5-9] These systems exploit the enhanced permeability and retention (EPR) effect for passive targeting and employ receptor-mediated transcytosis to actively cross the BBB. Moreover, novel stimuli-responsive delivery platforms enable precise drug release triggered by the TME's distinctive pH, redox gradients, or enzymatic activity.[10-12]

Despite these advances, significant challenges persist. Most nanocarriers are susceptible to rapid clearance by the mononuclear phagocyte system during systemic circulation, typically resulting in less than 1% of the administered dose reaching the tumor site[13]. In highly heterogeneous GBM, active targeting strategies often suffer from off-target effects. Furthermore, the subcutaneous xenograft models widely used in preclinical research fail to adequately recapitulate the physiological context of the BBB, contributing to repeated failures in translating promising animal study results to clinical applications. Additional concerns include the potential long-term toxicity and immunogenicity of carrier materials, as well as challenges in quality control for large-scale manufacturing. Thus, although drug delivery technologies offer renewed hope for glioma therapy, the field remains at a critical juncture, needing to overcome these persistent barriers to achieve successful clinical translation.

Against this backdrop, the research output in glioma drug delivery has grown rapidly, yet a systematic analysis of the global research landscape and its intellectual structure is lacking. Bibliometrics, a quantitative method that integrates mathematical statistics and visual analysis,

offers unique advantages in revealing disciplinary dynamics and tracing knowledge evolution. By systematically analyzing publication data within a field, it can objectively identify research trends, emerging topics, and knowledge trajectories. Since the early statistical analyses of publications in the 20th century and the formal introduction of the term "bibliometrics" by Pritchard in 1969,[14] the field has developed a robust theoretical framework. The advent of specialized tools such as VOSviewer and CiteSpace has further strengthened the role of bibliometrics in mapping knowledge structures. Bibliometric analysis generally encompasses two dimensions: performance analysis (assessing the impact of countries, institutions, authors, and journals) and science mapping (using methods like keyword co-occurrence and document co-citation to reveal knowledge associations and structural evolution). Its capacity to provide objective quantitative evidence and reduce researcher bias has established bibliometrics as a vital tool for forecasting trends across diverse fields, including medicine and environmental science. For example, researchers have employed bibliometric methods to examine the intersection of ChatGPT with traditional medicine,[15] analyze global trends in T cells and atherosclerosis,[16] predict hotspots in immunotherapy for atherosclerosis,[17] and conduct mapping analyses of sustainable biofuel economies.[18]

Given the absence of a systematic, quantitative overview of the rapidly evolving field of glioma drug delivery, this study conducts, for the first time, a comprehensive bibliometric and visual analysis. Utilizing tools including VOSviewer and R, we systematically investigate publication growth trajectories, international collaboration networks, institutional and journal contributions, author collaboration patterns, and keyword co-occurrence characteristics. The aim is to construct an integrated knowledge map, uncover research hotspots and evolutionary pathways, and provide evidence-based insights to help the academic community navigate the field's progress and optimize future research directions.

2 Material and methods

2.1 Data Source and Search Strategy

The data for this study were retrieved from the Web of Science Core Collection (WoSCC) database. A systematic literature search was conducted on April 3, 2026, covering the period from January 1, 2015, to December 31, 2025. The search employed the Topic (TS) field, which scans titles, abstracts, author keywords, and Keywords Plus®. The specific Boolean query used was: TS=(("glioma" OR "glioblastoma" OR "GBM")) AND TS=("drug delivery"). This strategy was designed to comprehensively capture literature relevant to both glioma and drug delivery research. The initial search results were screened based on the following criteria: only documents of the type "Article" were included to focus on original research and was limited to English-language publications. All records meeting these criteria were exported from WoSCC in "Plain Text" format with the "Full Record and Cited References" option selected. This ensures that each

record contains complete bibliometric information—including authors, title, abstract, citation data, and references—necessary for subsequent analyses such as co-citation.

2.2 Data analysis and Visualization software

A multi-software integrative approach was adopted to ensure a robust and comprehensive bibliometric analysis. WPS Office 365 was used for data preprocessing, descriptive statistics, and trend visualization. VOSviewer (version 1.6.20) was employed to construct collaboration, keyword co-occurrence, and co-citation networks, with full counting applied for all network analyses. CiteSpace (version 6.4.R1) was utilized for burst detection, co-citation clustering, and timeline analysis to identify research frontiers and thematic evolution. The Bibliometrix package (version 5.0) in R 4.5.0 was used to calculate scientometric indices (e.g., h-index, g-index), analyze core journals and author productivity, and generate Sankey diagrams. This strategy mitigates the limitations of individual tools, enables result cross-validation, and supports a multi-dimensional interpretation of the glioma drug delivery research landscape.

2.3 Analysis of Publication Output and Trends

Bibliometric analysis was performed using the bibliometrix package and its biblioshiny interface. The Main information function under the Overview tab was used to extract 12 core metrics (e.g., total articles, average citations per article, total authors, average articles age, single-authored documents, collaboration index) to assess the scope and composition of the dataset. The Annual Scientific Production function was applied to calculate the number of articles per year. The resulting data were exported to WPS Spreadsheets to generate a line chart illustrating trends in annual article numbers, revealing the temporal distribution and evolution of academic output in the field.

2.4 Analysis of Countries

The top 10 countries with the highest number of articles were identified using the Corresponding Author's Countries and Most Cited Countries functions in Bibliometrix. The Countries' Scientific Production function was applied to generate maps of scientific production by country and to perform co-authorship network analysis among different countries and regions. A country co-authorship network was also constructed in VOSviewer, with a thesaurus file used to unify the names of the same country, including standardizing regional designations (e.g., listing Taiwan as part of China in accordance with the Web of Science category). Only countries with at least 6 articles were included in the network.

2.5 Analysis of Author Keywords and Keywords Plus

Author keywords and Keywords Plus were analyzed using the Most Frequent Words function in Bibliometrix, and word cloud networks were generated via the WordCloud function. The Trend Topics function was used to analyze the evolution of major research themes over time, and the

Thematic Map function in the Clustering module was applied to generate thematic maps for Author Keywords and Keywords Plus, respectively. Co-occurrence networks of Author Keywords and Keywords Plus were constructed in VOSviewer using a thesaurus file to merge synonymous keywords (e.g., unifying "glioblastoma (gbm)" into "glioblastoma", and combining "blood-brain barrier (bbb)" and "blood brain barrier" into "blood-brain barrier"). The minimum occurrence threshold for keywords was set to 5.

2.6 Analysis of Journals

The top 10 journals by publication volume and citation impact were analyzed using the Most Relevant Sources and Most Local Cited Sources functions under the Sources section of Bibliometrix. Bradford's Law function was applied to identify the core sources in the field.

2.7 Multidimensional Analysis of Journal Influence

The top 10 journals related to the field of glioma drug delivery were analyzed using the Sources' Local Impact function under the Sources section of Bibliometrix. The Three-Field Plot function under the Overview section was used to explore the relationship among top author keywords, top authors and top journals. VOSviewer was employed to construct the bibliographic coupling map of journals, with a minimum of 6 occurrences per source.

2.8 Analysis of Institutions

VOSviewer was used to perform bibliographic coupling analysis of institutions, with the minimum number of documents of an organization set to 10.

2.9 Analysis of Authors

The top 20 authors in glioma drug delivery were identified and evaluated using the Authors' Local Impact function in the Bibliometrix package. The Authors' Production over Time function was used to analyze temporal trends in their annual publication output. The Author Profile function was applied to assess core author performance, including publication number, citation impact, and research continuity. The Three-Field Plot function in the Overview module was used to generate a Sankey diagram visualizing relationships among top authors, key author keywords, and high-productivity countries.

2.10 Citation Analysis

The top 10 cited publications related to the field of glioma drug delivery were identified using the Most Global Cited Documents function under the Documents section of Bibliometrix. CiteSpace was used to conduct co-citation reference clustering and timeline co-occurrence map analysis, with time slicing from January 2015 to December 2025, 1 year per slice. The node type was set to Reference, link strength to Cosine, link scope to Within Slices, and selection criteria to g-index with scale factor k=6. Additional parameters were LRF=2.5, L/N=10, LBY=5, and e=1.0.

VOSviewer was employed to analyze and construct the global citation network, with the minimum number of citations of a cited reference set to 38 and the top 50 citations retained.

3 Results

3.1 Bibliometric Analysis of Publication Output and Trends

Fig. 1A presents the key bibliometric characteristics of the field from 2015 to 2025. This corpus comprised 446 journals, which collectively yielded a total of 2,026 articles. The annual growth rate reached 6.39%, indicating vigorous development. A total of 11,135 authors contributed to this literature. Notably, only 7 articles were single-authored, with an average of 8.39 co-authors per article and an international collaboration rate of 25.81%. These metrics underscore a research landscape characterized by extensive teamwork and significant global cooperation. The breadth of research themes was reflected in the identification of 4,037 distinct author keywords. Regarding the foundational knowledge and academic impact, the articles collectively referenced 72,644 references and received an average of 34.34 citations per article, demonstrating a solid knowledge base and considerable scholarly influence. The mean article age was 5.52 years, pointing to a focus on recent research and confirming the field's rapid, ongoing evolution.

To further examine the article output and its evolutionary trajectory, a time-series analysis of the number of articles per year from 2015 to 2025 was performed (Fig. 1B). The number of articles exhibited a dynamic growth throughout this period. Specifically, the annual output stood at 133 in 2015, followed by a marked increase to 148 in 2016. From 2016 to 2021, the output maintained a steady upward trend, rising progressively from 148 to a peak of 211 in 2021. A subsequent decline was observed in 2023, with the number of articles falling to 186. Notably, the field rebounded strongly in 2024 and 2025, reaching 200 and 247, respectively. Collectively, these data demonstrate a sustained long-term growth in annual article output, underscoring the continuous expansion of research interest and activity within the field.

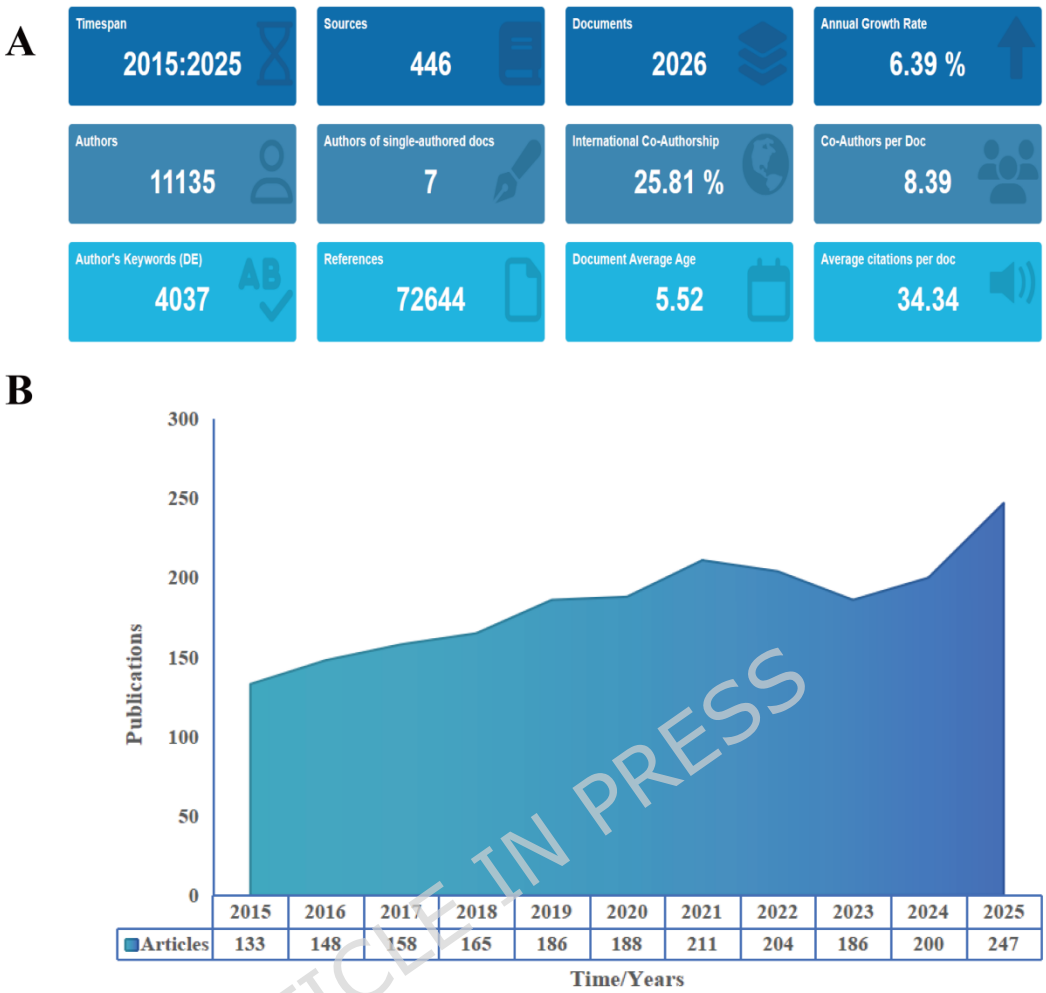

Fig. 1 Quantitative analysis of article output and publication trends. (A) The Characteristics of Bibliometrics. (B) Annual number of articles.

3.2 Bibliometric Analysis of Countries

To assess the scientific contributions and influence of different countries in glioma drug delivery research, this study analyzed the the publication output and collaborative patterns of countries. As shown in Tab. 1, China holds a dominant position in terms of publication volume, contributing 811 articles which account for 40.00% of the total articles. These articles have received 33,684 citations, with an average of 41.50 citations per article. The USA ranks second, with 291 articles, 13,034 total citations, and a similar average of 44.08 citations per article.

Tab. 1 Top 10 countries with the highest number of articles

Country	Article	Articles %	SCP	MCP	MCP%	Total Citations	Average Article Citations
China	811	40	714	97	12	33684	41.50
USA	291	14.4	215	76	26.1	13034	44.80
India	118	5.8	92	26	22	2944	24.90
Italy	78	3.8	54	24	30.8	1984	25.40
Iran	77	3.8	54	23	29.9	1993	25.90
Korea	64	3.2	51	13	20.3	2092	32.70
Brazil	52	2.6	36	16	30.8	1217	23.40
United Kingdom	50	2.5	27	23	46	1219	24.40
Canada	34	1.7	18	16	47.1	1122	33.00
France	34	1.7	12	22	64.7	1084	31.90

Notes: Abbreviations: SCP, same-country collaboration; MCP, multi-country collaboration papers.

Fig. 2A visualizes the global distribution of country-level articles, with color intensity reflecting research output volume. China, shaded in the darkest blue, is the most productive nation, leading global research in this field. The United States, marked by a medium-dark blue, is another major contributor, while multiple European, Asian, South American, and Oceanian countries show moderate to high output in light to medium blue. Most African, Central Asian, and parts of American nations are grey, indicating limited or no research activity. Overall, article output is highly geographically uneven, concentrated in North America, Europe, and East Asia, with China and the USA as the core contributors, reflecting global disparities in research resources and investment. The collaboration network among countries/regions with at least 5 articles was visualized using VOSviewer (Fig. 2B). In this network, node size corresponds to a country's article count, link thickness indicates collaboration strength, and colors represent different collaborative clusters. The results reveal a significant imbalance in geographical research output, characterized by a pronounced "top-concentration effect." Specifically, the majority of research achievements are concentrated in a limited number of countries, led by China and the United States.

3.3 Bibliometric Analysis of Author Keywords and Keywords Plus

Keywords serve as essential indicators for identifying research hotspots and knowledge structures in a field. "Author Keywords" reflect the core content of studies, while "Keywords Plus" capture broader thematic associations derived from citation networks. High-frequency keyword analysis (Tab. 2) identifies "glioblastoma" and "drug delivery" as the central research themes. The top Author Keywords are "glioblastoma" (n = 882), "drug delivery" (n = 337), "blood-brain barrier" (n = 368), and "temozolomide" (n = 108), "nanoparticles" (n = 107), delineating the field's core mission: developing nanoparticle delivery systems for agents like temozolomide to target gliomas, with a primary focus on overcoming the blood-brain barrier. The Keywords Plus list provides broader contextual insight, with "drug delivery" (n = 792), "nanoparticles" (n = 526), and "glioblastoma" (n = 409) being most prominent. Integrating these with Author Keywords indicates a strong convergence with nanotechnology and positions the research within the wider

scope of cancer therapy. The high frequency of terms such as “in-vitro”, “therapy”, and “cells” further reflects a current emphasis on preclinical and translational studies.

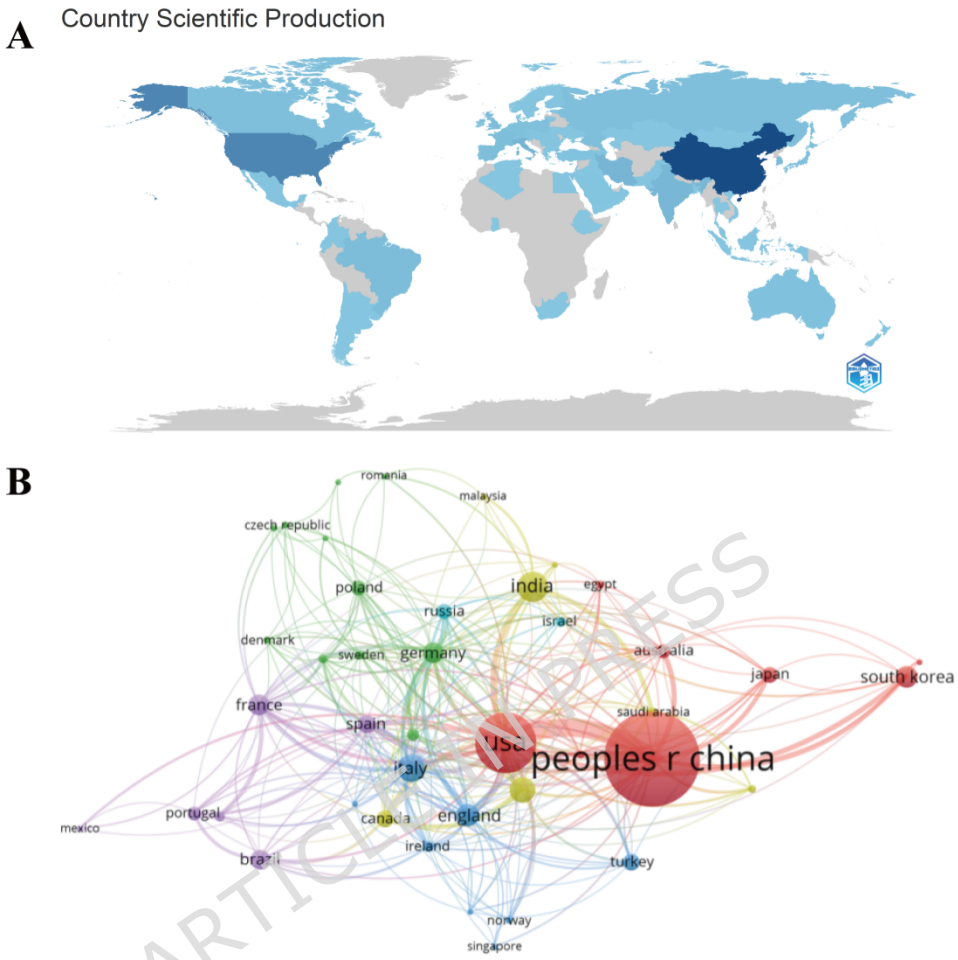

Fig. 2 Bibliometric analysis of contributing countries. (A) Articles by country. (B) Co-authorship network analysis among different countries.

Tab. 2 Frequency of Author Keywords and Keywords Plus

Author Keywords	Frequency	Keywords Plus	Frequency
glioblastoma	882	drug delivery	792
drug delivery	337	nanoparticles	526
blood-brain barrier	368	glioblastoma	409
temozolomide	108	cancer	298
nanoparticles	107	in-vitro	293
doxorubicin	99	therapy	258
nanomedicine	71	blood-brain barrier	232
liposomes	67	delivery	221
targeted drug delivery	54	cells	203
paclitaxel	52	doxorubicin	167
brain tumor	51	temozolomide	162
chemotherapy	48	paclitaxel	136
cancer	45	brain	131
focused ultrasound	45	release	129
apoptosis	40	expression	122

Visualizations of keyword frequency and trends are presented in Fig. 3. Word clouds (Fig. 3A and 3B) visually represent the occurrence rates of Author Keywords and Keywords Plus. The "Trend Topics" analysis (Fig. 3C) reveals the temporal evolution of research themes, showing clear chronological shifts in focus. The latest hotspots (2024–2025) include glioblastoma, molecular docking, drug resistance, and ferroptosis, while exosomes and immunotherapy peaked in 2022–2023 as sustained high-interest themes. Foundational topics like nanoparticles, drug delivery, and temozolomide reached their peak around 2020–2021, with early-stage themes (e.g., glioblastoma, paclitaxel) prominent in 2018–2019. glioblastoma remain core themes across the entire period.

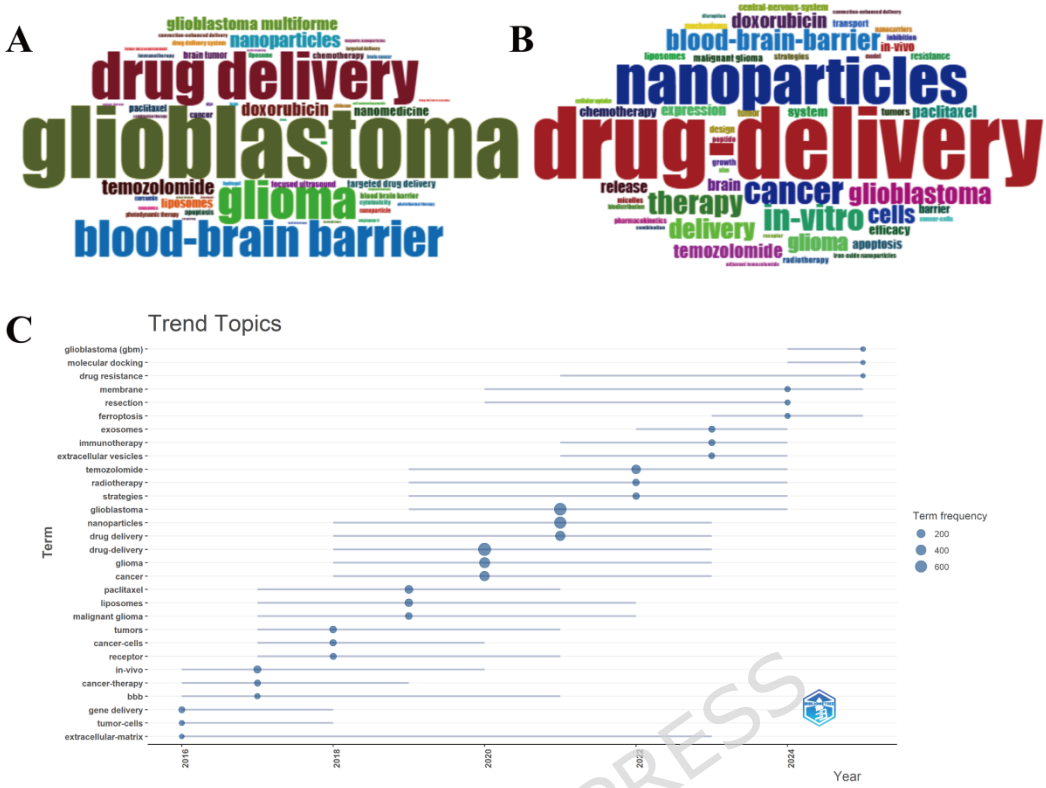

Fig. 3 Analysis of keyword frequency and research trends. (A) Word cloud of author keywords. (B) Word cloud of Keywords Plus. (C) Trend topics showing the evolution of major research themes over time.

A thematic strategic diagram (Fig. 4A) categorized research themes into four quadrants based on centrality (relevance) and density (development). The Basic Themes (high centrality, low density) are the field's foundational topics, including glioblastoma, drug delivery, BBB, apoptosis, and chitosan. The Motor Themes (high centrality, high density) are the field's driving hotspots, such as convection-enhanced delivery, drug delivery systems, focused ultrasound, and nanocarrier. The Niche Themes (low centrality, high density) are specialized subfields, including polymeric micelles, microfluidics, and pH-responsive systems. The Emerging or Declining Themes (low centrality, low density) include local drug delivery, extracellular vesicles, and photodynamic therapy. Correspondingly, the Keywords Plus thematic analysis (Fig. 4B) also identified four distinct theme types. The Basic Themes (high centrality, low density) include core topics such as drug-delivery, nanoparticles, cancer, design, micelles, nanocarriers, glioblastoma, central-nervous-system, and radiotherapy. Co-occurrence networks for both keyword sets are shown in Fig. 4C and 4D, where node attributes represent publication year, frequency, and co-occurrence strength. Analysis of 4,029 Author Keywords and 3,446 Keywords Plus revealed prominent nodes: in the Author Keywords network, "glioblastoma" (link strength: 1,248), "blood-brain barrier" (829), and "drug delivery" (739) are central; in the Keywords Plus network, "drug delivery" (4,376), "nanoparticles" (2,833), and "in-vitro" (1,766) dominate.

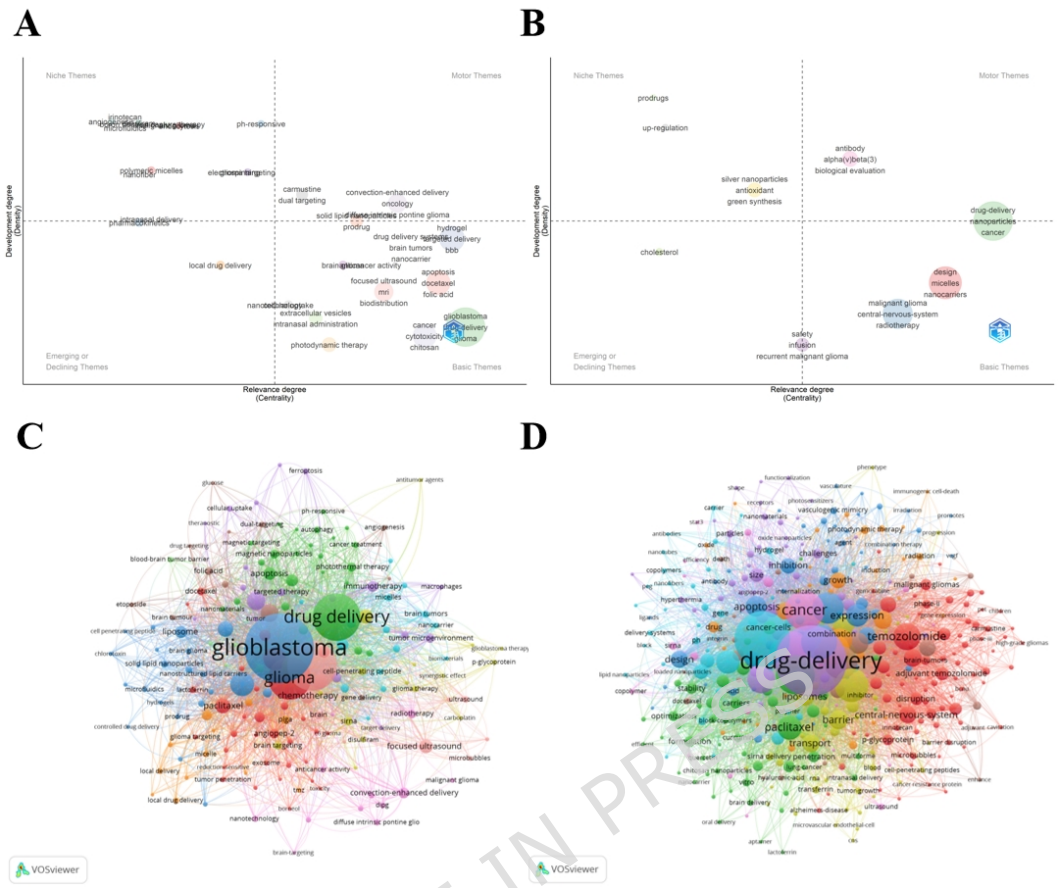

Fig. 4 Bibliometric analysis of Author Keywords and Keywords Plus. (A) The thematic map of Author Keywords (minimum occurrence: 5 for both Author Keywords and Keywords Plus). (B) The thematic map of Keywords Plus. (C) The co-occurrence network of Author Keywords. (D) The co-occurrence network of Keywords Plus.

3.4 Bibliometric Analysis of Journals

Analysis of journal distribution showed that publications in glioma drug delivery were concentrated in interdisciplinary journals covering biomedicine, materials science, and drug delivery. As shown in Tab. 3 and Fig. 5, the *Journal of Controlled Release* was the most productive with 101 articles, followed by *ACS Applied Materials & Interfaces* (68) and *Pharmaceutics* (63). Although *Biomaterials* ranked eighth in publication number (38 articles), it achieved the highest average citation rate (94.76), demonstrating outstanding academic impact. *ACS Nano* also presented high influence with an average of 61.22 citations per article.

Tab. 3 Top 10 Journals by Publication Volume and Citation Impact

Rank	source	Articles	citations	Average
1	Journal of Controlled Release	101	4331	42.88
2	ACS Applied Materials & Interfaces	68	1217	17.90
3	Pharmaceutics	63	792	12.57
4	International Journal of Pharmaceutics	57	1863	32.68
5	International Journal of Nanomedicine	50	1433	28.66
6	Journal of Drug Delivery Science and Technology	40	312	7.80
7	Molecular Pharmaceutics	39	1096	28.10
8	Biomaterials	38	3601	94.76
9	ACS Nano	32	1959	61.22
10	International Journal of Molecular Sciences	30	1433	47.77

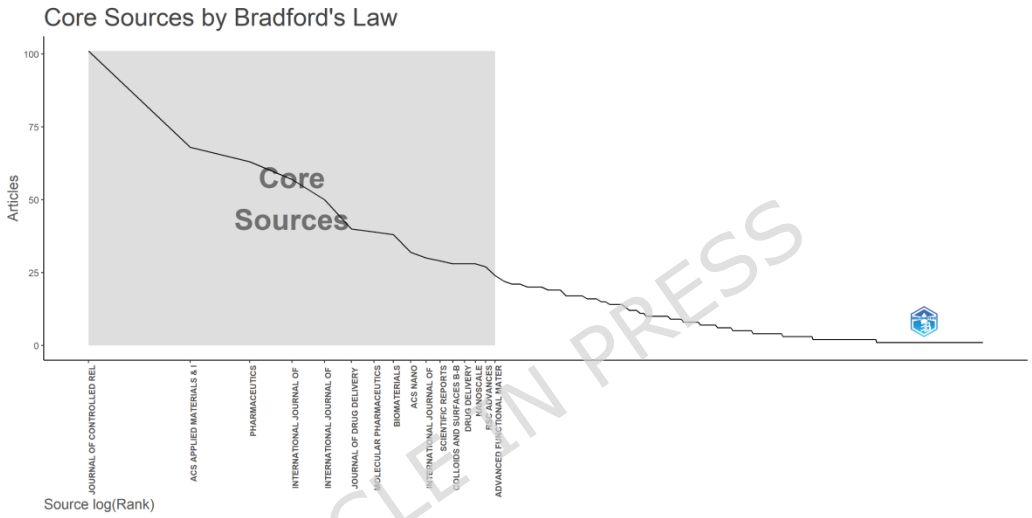

Fig. 5 Core sources identified by Bradford's Law.

3.5 Multidimensional Analysis of Journal Influence

To quantitatively assess the academic influence of journals in this field while overcoming the limitations of single-metric evaluation, this study employs a comprehensive set of scientometric indicators, including the h-index, g-index, m-index, total citations (TC), and number of publications (NP). The h-index—originally designed to measure a researcher's output and impact—is applied here to journal evaluation. It represents the highest number h such that a journal has h papers each cited at least h times, thereby reflecting both the productivity and impact of its publications. The g-index complements the h-index by giving more weight to highly cited articles; it is the largest number g where the top g articles have collectively received at least g^2 citations. The m-index, derived from the h-index, is calculated as the h-index divided by the number of years since the journal's first relevant publication, offering a normalized measure of the annual growth of influence. As shown in Tab. 4, multi-indicator analysis reveals distinct profiles among core journals. In terms of publication volume, the *Journal of Controlled Release* (2024 IF = 11.5) leads substantially with 101 articles, far ahead of *ACS Applied Materials &*

Interfaces (68 articles; 2024 IF = 8.2) and the *International Journal of Pharmaceutics* (57 articles; 2024 IF = 6.4), underscoring its central role in the field. Regarding citation-based impact, the *Journal of Controlled Release* also ranks highest among the top ten in three key metrics: an h-index of 46, a g-index of 70, and a total citation count of 5,209, confirming the sustained academic value and recognition of its published research. In contrast, *Journal of Controlled Release* achieves the highest m-index (3.833), indicating a rapid accumulation of influence within a relatively short active period.

Further analysis of the top 10 journals reveals distinct strategic strengths. While International *Journal of Nanomedicine* (NP=50, TC=2143) and *Biomaterials* (NP=38, TC=3156) publish fewer articles than the top-ranked journals, they maintain strong impact metrics, highlighting a balance between publication volume and citation efficiency. Notably, *ACS Nano* (NP=32, TC=3474) achieves the third-highest total citations among the top 10, demonstrating exceptional per-article impact.

Tab. 4 Top 10 Journals Related to the Field of Glioma Drug Delivery

Journal	NP	h_index	g_index	m_index	TC
Journal of Controlled Release	101	46	70	3.833	5209
ACS Applied Materials & Interfaces	68	39	60	3.25	3669
International Journal of Pharmaceutics	57	31	48	2.583	2409
Biomaterials	38	30	38	2.5	3156
International Journal of Nanomedicine	50	29	46	2.417	2143
Drug Delivery	28	23	28	1.917	1536
Molecular Pharmaceutics	39	23	33	1.917	1147
ACS Nano	32	21	32	1.75	3474
Advanced Materials	22	20	22	1.667	1779
Nanoscale	28	20	28	1.667	1682

Notes: Abbreviations: NP, number of publications; TC, total citations.

The relationships among major keywords, leading authors, and prominent journals are further visualized in Sankey diagram (Fig. 6A). The journal bibliographic coupling network included 446 journals that shared at least one cited reference. As shown in Fig. 6B (minimum number of documents per source: 6), the *Journal of Controlled Release* ranked first with a total link strength of 27,801, followed by *ACS Applied Materials & Interfaces* (15,729) and the *International Journal of Pharmaceutics* (11,729). The strongest single linkage exists between the *Journal of Controlled Release* and *ACS Applied Materials & Interfaces*, with a link strength of 2,034.

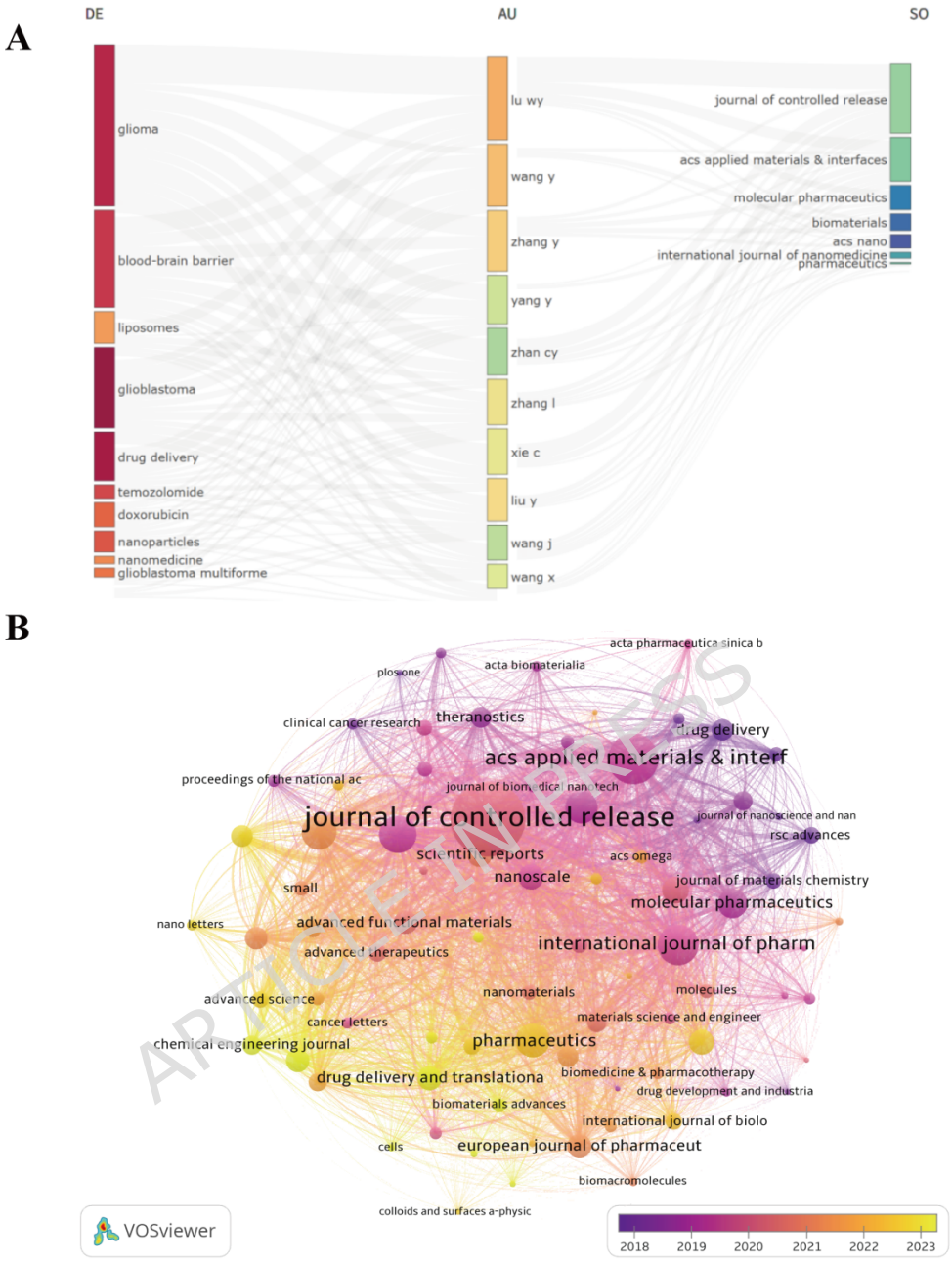

Fig. 6 Bibliometric analysis of journals. (A) The relationship among top author keywords, top authors and top journals summarized by a Sankey three-field plot. (B) The bibliographic coupling map of journals.

3.6 Bibliometric Analysis of Institutions

To evaluate the contributions and collaborative influence of research institutions in the field of glioma drug delivery, a bibliographic coupling analysis was performed. As shown in Tab. 5, the top 10 institutions account for approximately 10.85% of total articles, with 9 based in China, demonstrating China's leading role in the field. Fudan University tops the list with 99 articles and 5,588 citations, followed by the Chinese Academy of Sciences (65 articles, 4,130 citations) and

Sichuan University (54 articles, 3,093 citations). Johns Hopkins University, the only non-Chinese institution in the top 10, ranks 9th with strong international collaboration. Overall, research in this field is highly concentrated in leading Chinese academic institutions. The institutional collaboration network, illustrated in Fig. 7, includes 80 institutions that met the threshold of at least 10 articles, out of a total of 2,487 identified. Within this network, the Chinese Academy of Sciences demonstrates the highest total link strength (79), indicating its central role in knowledge exchange, followed by Chang Gung University (67) and Fudan University (51).

Tab. 5 Top 10 institutions related to the Field of Glioma Drug Delivery

Institution	Articles	citations	total link strength	Country
Fudan University	99	5588	51	China
Chinese Academy of Sciences	65	4130	79	China
Sichuan University	54	3093	12	China
Shanghai Jiao Tong University	45	2127	34	China
Zhejiang University	34	913	19	China
Chang Gung University	29	1216	67	China
Nanjing Medical University	28	875	29	China
Soochow University	28	1843	22	China
Johns Hopkins University	28	786	13	United States
Xuzhou Medical University	25	726	12	China

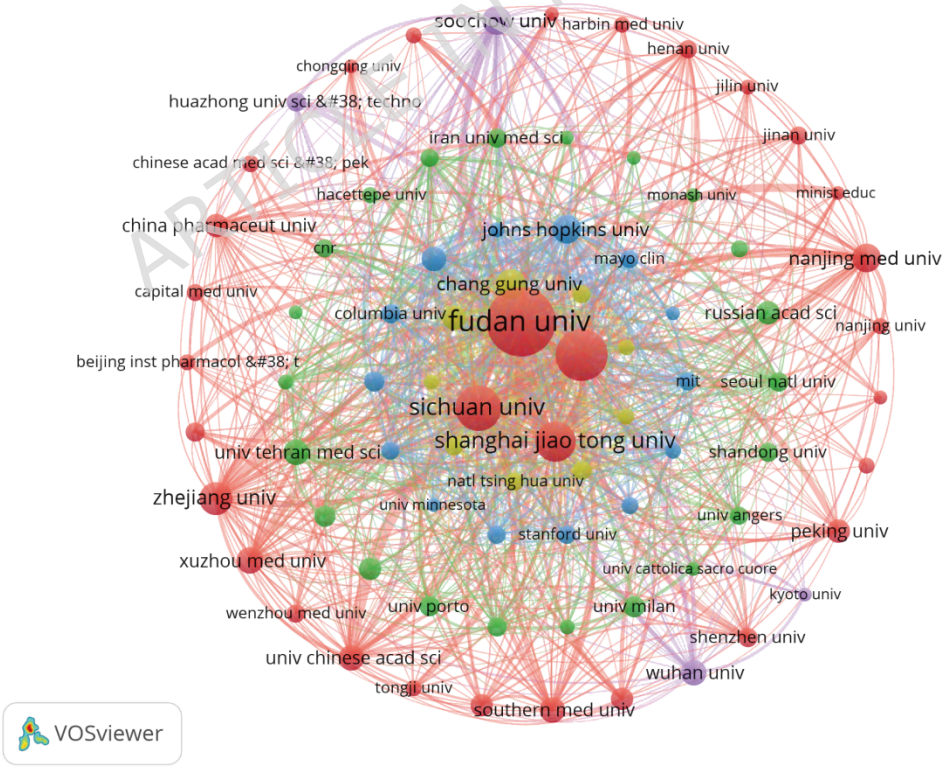

Fig. 7 The bibliographic coupling map of institutions (minimum number of documents per organization: 10).

3.7 Bibliometric Analysis of Authors

A detailed assessment of article output and academic impact further highlights the leading researchers within this community. As summarized in Tab. 6, which lists the top 20 authors by publication volume alongside metrics such as the h-index, g-index, m-index, and total citations (TC), LU WY emerges as the most prominent scholar. LU WY leads in multiple categories, including number of articles (46), h-index (29), total citations (2,447), and m-index (2.417), reflecting outstanding productivity and sustained influence relative to career length. Other authors, such as WANG Y and XIE C, also demonstrate strong performance, collectively forming a highly productive core group that underpins the field's research activity.

Tab. 6 Top 20 authors related to the Field of Glioma Drug Delivery

Author	NP	h_index	g_index	m_index	TC	PY_start
LU WY	46	29	46	2.417	2447	2015
WANG Y	43	21	43	1.75	1884	2015
XIE C	25	20	25	1.667	1431	2015
ZHAN CY	22	20	22	1.667	1635	2015
ZHANG Y	35	20	35	1.667	1525	2015
ZHANG L	28	18	28	1.5	1917	2015
LIU Y	29	16	25	1.333	669	2015
WANG H	20	16	20	1.333	927	2015
YANG Y	23	16	23	1.455	854	2016
LIU X	17	15	17	1.25	936	2015
WANG J	22	15	22	1.364	1098	2016
CHEN J	15	14	15	1.167	948	2015
CHEN X	18	14	18	1.273	731	2016
GAO HL	16	14	16	1.167	1854	2015
HE Q	16	14	16	1.167	1709	2015
WANG X	24	14	24	1.167	906	2015
CHEN JP	16	13	16	1.3	519	2017
SUN Y	14	13	14	1.083	649	2015
WANG Z	18	13	18	1.083	555	2015
ZHANG Q	14	13	14	1.182	392	2016

Notes: Abbreviations: NP, number of publications; TC, total citations.

The dynamic evolution of author output and influence is visualized in Fig. 8A, which illustrates annual articles and citation trends for selected authors from 2015 to 2025. The figure reveals distinct temporal patterns, with some authors showing concurrent peaks in productivity and impact, while others maintain steady contributions over time. Furthermore, the interrelationships among leading authors, their affiliated countries/regions, and core research themes are depicted in the Sankey diagram (Fig. 8B). Among the top 20 authors, “glioma” appears as the most frequently associated keyword, underscoring its central thematic role within this influential cohort.

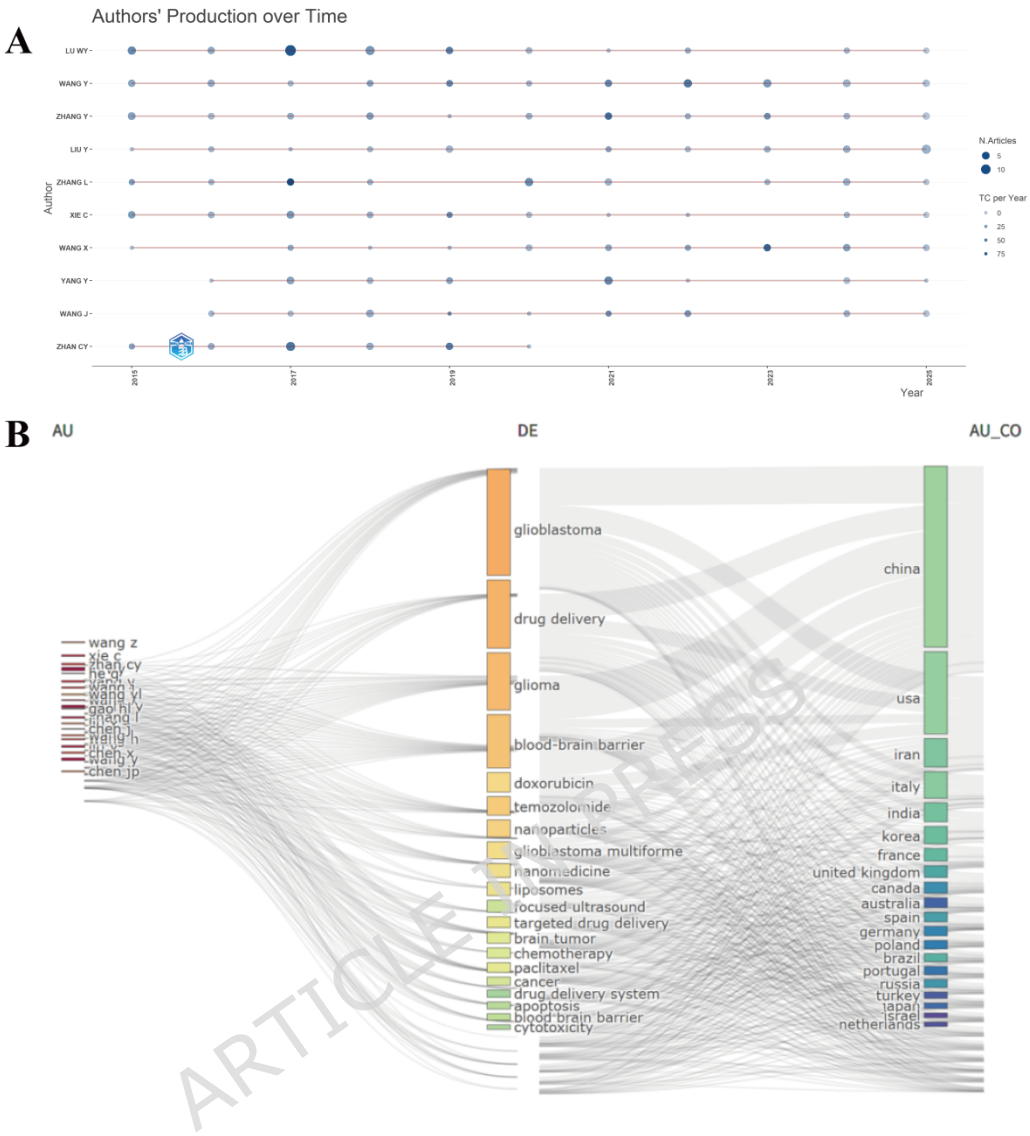

Fig. 8 Bibliometric analysis of authors. (A) Top 20 authors' production over time. (B) The relationship among top authors, top country/region and top author keywords summarized by a Sankey three-field plot.

3.8 Citation Analysis

Citation analysis was performed to evaluate the academic impact of articles using the Bibliometrix R package based on the Web of Science Core Collection (WoSCC) database (2015–2025). As shown in Tab. 7, the top-cited article was by XUE JW (2017, *Nature Nanotechnology*), with 796 total citations, representing a foundational contribution to glioma drug delivery.

Tab. 7 Top 10 cited articles related to the Field of Glioma Drug Delivery

Paper	DOI	Total Citations	TC per Year	Normalized TC
XUE JW, 2017, NAT NANOTECHNOL	10.1038/NNANO.2017.54	796	79.60	14.20
JIA G, 2018, BIOMATERIALS	10.1016/j.biomaterials.2018.06.029	601	66.78	10.37
HARASZTI RA, 2016, J EXTRACELL VESICLES	10.3402/jev.v5.32570	566	51.45	9.87
YANG ZG, 2020, NAT BIOMED ENG	10.1038/s41551-019-0485-1	563	80.43	13.21
ZHENG M, 2015, ACS NANO	10.1021/acsnano.5b05575	469	39.08	7.47
LIN TT, 2016, ACS NANO	10.1021/acsnano.6b04268	421	38.27	7.34
ZHANG HY, 2021, SCI ROBOT	10.1126/scirobotics.aaz9519	384	64.00	11.34
LI SH, 2020, NAT BIOMED ENG	10.1038/s41551-020-0540-y	320	45.71	7.51
CHAI ZL, 2019, ACS NANO	10.1021/acsnano.9b00661	306	38.25	6.31
FAN KL, 2018, ACS NANO	10.1021/acsnano.7b06969	299	33.22	5.16

To further deconstruct the knowledge base, a co-citation analysis was conducted. Co-citation analysis in Fig. 9A identified 7 core thematic clusters in glioma drug delivery research. Cluster #1 (brain tumor) and Cluster #0 (blood-brain barrier) represent the field's central clinical focus and core translational challenge, respectively. Cluster #2 (biomimetic nanoparticle) and Cluster #3 (glioblastoma multiforme) highlight cutting-edge delivery technologies and disease-specific research priorities. Cluster #4 (focused ultrasound) and Cluster #5 (drug delivery) delineate specialized technical subfields and foundational engineering research. This network comprehensively maps the field's intellectual structure and research frontiers.

The temporal evolution of these themes is systematically displayed in the co-citation timeline map (Fig. 9B). A clear developmental sequence is evident: research during 2010–2017 focused primarily on foundational tumor microenvironment and CNS biology; the period 2015–2019 shifted toward GBM-specific therapy and controlled-release carrier design; and from 2019–2025, the emphasis expanded to the cutting-edge frontier of engineered exosome-mediated delivery. Together, these analyses confirm the field's trajectory from initial biological and carrier-focused research toward advanced, targeted delivery strategies. The intrinsic link between glioma pathology and the blood-brain barrier remains the enduring focus of research. The global citation network is further illustrated in Fig. 10.

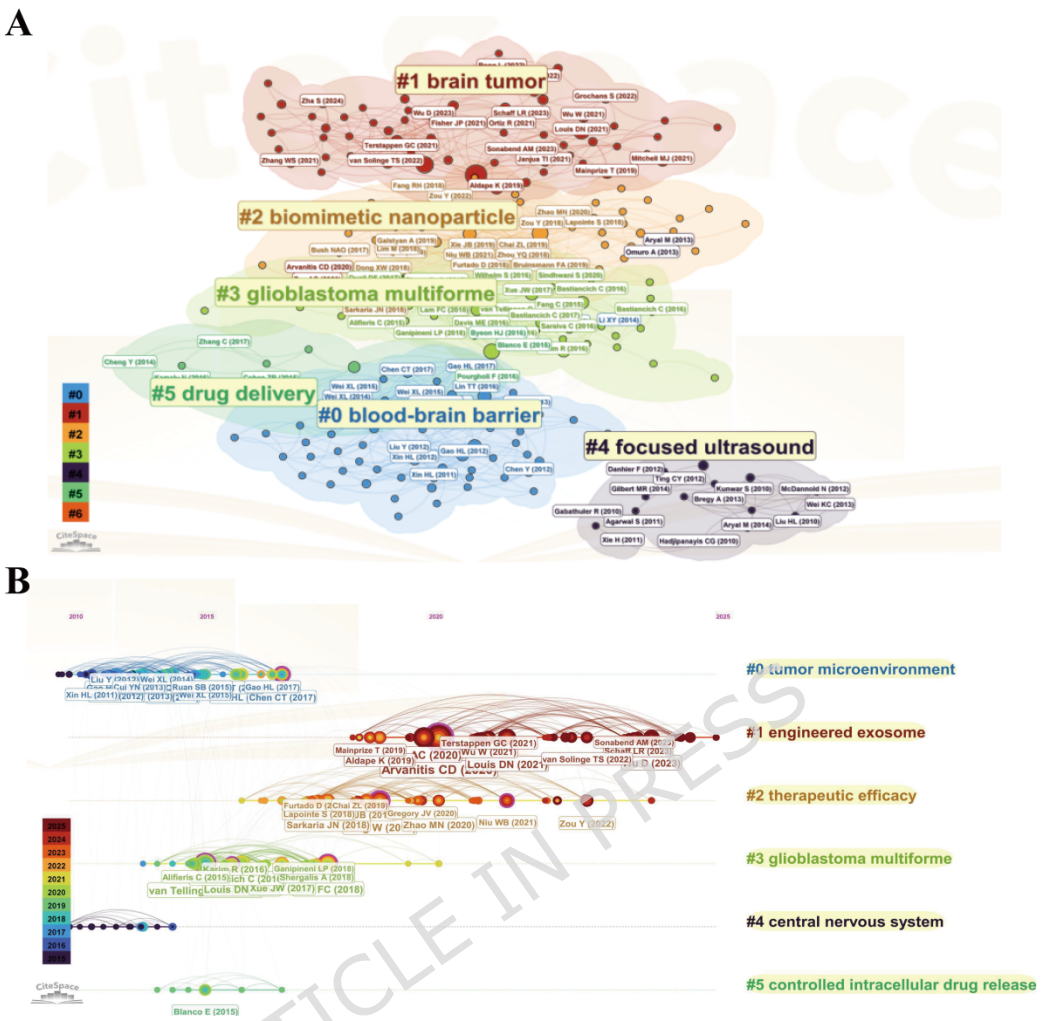

Fig. 9 Bibliometric analysis of citation. (A) Co-citation reference clustering. (B) Timeline map. Time span: 2015-2025 (Slice Length=1), Selection Criteria: g-index (k=6), LRF=2.5, L/N=10, LBY=5, e=1.0; Network: N=270, E=1021 (Density=0.0281); Largest 1 CCs: 263 (97%); Nodes Labeled: 1.0%; Pruning: None.

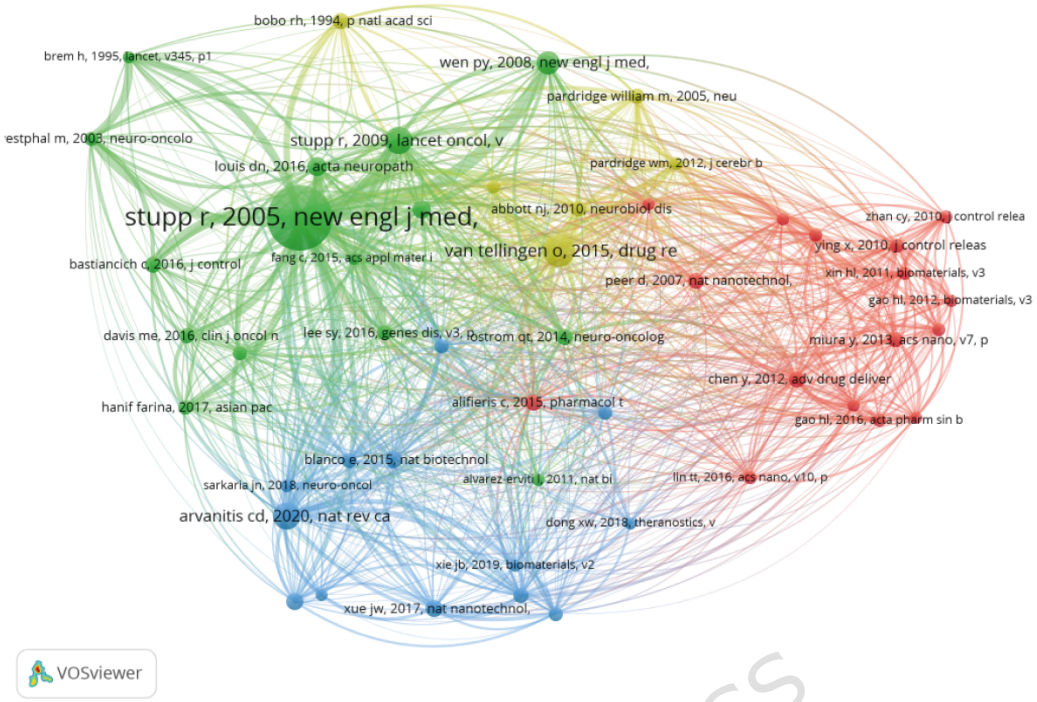

Fig. 10 The bibliographic coupling map of global citation (minimum number of citations of a cited reference: 38; top 50 citations retained).

4 Discussion

This bibliometric study delineates the global landscape and evolutionary trends of glioma drug delivery research from 2015 to 2025, demonstrating vigorous academic development, geographically concentrated contributions, and a clear shift toward precision translational medicine. The steady annual publication growth and high international collaboration rate illustrate strong global investment and extensive cross-border teamwork in this field. The dominant research output from China and the United States, with most top-performing institutions located in China, reveals an East-West dual-core collaborative pattern that supports efficient resource integration and disciplinary progress.

Keyword and co-citation analyses consistently identified the blood-brain barrier and glioblastoma as the central themes across the decade (Tab. 2; Fig 9A), confirming that overcoming BBB limitations and developing nanocarrier-mediated targeted chemotherapy constitute the core goals of glioma drug delivery research. This finding directly aligns with the co-citation cluster #0 (blood-brain barrier) and cluster #1 (brain tumor) shown in Fig 9A, which represent the field's most enduring intellectual hubs. Trend topic analysis (Fig. 3C) revealed a clear evolutionary trajectory: conventional nanocarrier design and chemotherapy dominated the period from 2015 to 2019; exosomes and immunotherapy emerged as major research hotspots during 2020–2023; and molecular docking, drug resistance, and ferroptosis have become newly emerging frontiers from 2024 to 2025. These temporal shifts are further corroborated by the keyword burst detection, which identified "exosomes" as the strongest burst term between 2020

and 2023, and “ferroptosis” as an emerging burst after 2024. The thematic strategic diagram (Fig. 4A) categorizes “exosomes” and “immunotherapy” within the Motor Themes quadrant (high centrality and high density) for the 2020–2023 period, confirming their role as field drivers, whereas “ferroptosis” appears in the Emerging or Declining Themes quadrant for 2024–2025, indicating recent but still developing interest. Overall, the research focus has shifted from traditional drug delivery systems toward advanced directions such as extracellular vesicle therapy and immunotherapy, reflecting ongoing innovation in the field. The thematic strategic diagram further clarifies the intellectual structure of the discipline, with foundational themes providing a stable basis and motor themes driving continuous progress.

Co-citation clustering and timeline analysis (Fig. 9B) further delineated the developmental path of the field, progressing from basic studies on the tumor microenvironment and BBB biology (2015–2017), to targeted carrier design for glioblastoma (2017–2019), and finally to biomimetic delivery and immune-integrated therapeutic strategies (2019–2025). Importantly, the timeline map shows that cluster #2 (biomimetic nanoparticle) and cluster #4 (focused ultrasound) emerged around 2018–2019 and have sustained activity through 2025, consistent with the trend topics showing “engineered exosomes” and “cell membrane coating” as motor themes from 2020 onward. Notably, the *Journal of Controlled Release* was the most productive journal, while *Biomaterials* and *ACS Nano* showed the highest citation impact (Tab. 3, Tab. 4), collectively reflecting the highly interdisciplinary nature of this field, which integrates pharmaceutics, materials science, and neuro-oncology. The co-citation cluster #4 (focused ultrasound) and cluster #5 (drug delivery) further emphasize the technical diversity captured by our bibliometric analysis, including physical delivery methods alongside nanoparticle-based systems. These results underline the interdisciplinary features and core publication platforms in this research area. Research output and collaboration are concentrated among major institutions, particularly those in China (Tab. 5), collectively shaping the global landscape of glioma drug delivery. These multidimensional indicators also provide a quantitative reference for researchers in journal selection and for institutions in identifying core literature. In addition, highly productive core authors represented by LU WY have maintained consistent high-level output (Tab. 6), forming a stable academic backbone that supports the steady development of the field.

Current standard glioblastoma treatment remains constrained by disappointing survival rates, mainly due to BBB obstruction, complex TME, and drug resistance[19]. In contrast, DDS effectively enhance tumor drug accumulation, reduce systemic toxicity, and achieve controlled targeted delivery via receptor-mediated transcytosis, the EPR effect and stimuli-responsive release[20]. Post-2020 evidence suggests that optimized nanocarriers may offer potential improvements in delivery efficiency and therapeutic index compared with free drugs[21].

Commonly used biomaterials exhibit distinct trade-offs in glioma delivery: PLGA (biocompatible but poor BBB penetration)[22]; PEGylation (prolonged circulation but anti-PEG immunity)[23]; PCL/PLA (mechanical stability yet hydrophobicity and low drug loading)[24];

chitosan (BBB crossing but poor solubility and batch variability)[25]; hyaluronic acid (CD44-mediated targeting but rapid clearance)[26]; dendrimers (theranostic potential yet high cost and cytotoxicity)[27]; and PEI (strong gene condensation but poor biodegradability and toxicity)[28]. Since 2020, the field has shifted toward biomimetic carriers (e.g., engineered exosomes and cell membrane-coated nanocarriers) and multi-stimuli-responsive platforms, which show promising potential for BBB penetration and tumor microenvironment regulation[29, 30].

Future advances may center on AI-assisted carrier design and immunomodulatory delivery. AI can accelerate material and ligand screening, optimize nanocarrier performance, and reduce translational uncertainty[31]. Immunomodulatory DDS remodel the immunosuppressive TME and may improve combination therapy outcomes[32]. Engineered exosomes remain promising due to their superior biocompatibility and low immunogenicity[33]. However, key clinical translation challenges persist, including limited BBB crossing, tumor heterogeneity, batch consistency, long-term biosafety, and scalable production[34]. Moving forward, interdisciplinary integration of materials science, neuro-oncology, immunology, and AI will be essential to develop intelligent theranostic systems that bridge preclinical findings and clinical value.

5 Conclusion

This study aimed to systematically analyze the global landscape and evolutionary trends of glioma drug delivery research from 2015 to 2025 using bibliometric and visual methods. The field has shown steady growth and extensive international collaboration, with China and the United States as the dominant contributors. Research has been consistently centered on overcoming the blood-brain barrier for glioblastoma treatment, with a clear thematic shift from conventional nanocarriers and chemotherapy to biomimetic systems, exosomes, and immunotherapy. The discipline is highly interdisciplinary, supported by core journals and productive authors in pharmaceutics, materials science, and neuro-oncology. Future research may prioritize intelligent nanocarrier design, AI-assisted optimization, and immunomodulatory delivery to inform potential steps toward clinical translation.

Abbreviations

Full term	Abbreviation
glioblastoma multiforme	GBM
temozolomide	TMZ
blood-brain barrier	BBB
tumor microenvironment	TME
drug delivery systems	DDS
enhanced permeability and retention	EPR
Web of Science Core Collection	WoSCC
total citations	TC
number of publications	NP
same-country collaboration	SCP

multi-country collaboration papers	MCP
poly(ε-caprolactone)/polylactic acid	PCL/PLA
polyethylenimine	PEI

Declarations

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Author contributions

WY and XT: Investigation, Methodology, Formal analysis, Visualization, Data curation, Software, Writing – original draft preparation, and Writing – review and editing. XH and YL: Supervision, Writing – review and editing. DS, YC and SS: Funding acquisition, Supervision, Writing – review and editing. All authors have read and agreed to the published version of the manuscript.

Competing interests

The authors declare no competing interests.

Ethics approval

Not applicable.

Consent to participate

Not applicable.

Consent for publish

Not applicable.

Data availability

The data used to support the findings of this study are included within the article.

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